8EHQ_0504 - 15566S

Great Lakes
CHEMICAL CORPORATION

05 May 2004

VIA CERTIFIED MAIL
Internal ID #: 04-01

8EHQ-04-15566

Great Lakes Chemical Corporation
One Great Lakes Boulevard
West Lafayette, IN 47906 USA
P.O. Box 2200
West Lafayette, IN 47996-2200 USA

Telephone: (1) 765 497 6100
Facsimile: (1) 765 497 5400

www.greatlakes.com

Document Processing Center
Mail Code 7404
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

M2 275 192

RECEIVED
OPPT NCIC
04 MAY 10 AM 11:05

SANITIZED

Attention: TSCA Section 8(e) Coordinator

RE: Submission of Reproductive and Fetal Survival Effects in the Rat via an OECD 422 Guideline Screening Study of Phenol, isopropylated, phosphate (3:1); (CAS No.: 68937-41-7) [
].
(When responding, please refer to JAB-04-013).

THIS MAY BE SANITIZED

Dear Sir:

Great Lakes Chemical Corporation (GLCC) submits this letter of substantial risk notification in accordance with Section 8(e) of the Toxic Substances Control Act, 15 USC 2607(e), and the Environmental Protection Agency's "Statement of Interpretation and Enforcement Policy" thereof 43 FR 1110, 35 seq., March 16,1978. The notification is in regards to a verbal report and draft Summary Data Tables received from the laboratory that is performing an OECD 422 Combined Repeated Dose Toxicity Study with the Reproduction/ Developmental Toxicity Screening Test of isopropylated triphenyl phosphate (common name) [
].

RECEIVED
OPPT NCIC
2004 MAY 17 PM 2:18

The test material was administered via oral gavage using corn oil as the carrier vehicle to groups of 12 male and 12 female Sprague-Dawley Crl:CD®(SD)IGS BR strain of rat. The test material was given once daily at dose levels of 25, 100 or 400 mg/kg. Males were dosed for at least 14 days prior to mating and continued to be dosed throughout mating for a minimum of 28 days. Females were dosed for at least 14 days prior to mating, throughout mating and continued to be dosed until one day prior to termination (lactation day 4 for those that delivered, post-mating day 25 or post-cohabitation day 25 for those that did not deliver). A concurrent control group of identical design received the carrier vehicle corn oil on a comparable regimen.

The study design included recording F_0 viability and clinical observations, body weights and food consumption, functional observation battery, locomotor activity, clinical pathology, and parturition and litter observations. F_1 data included litter identification, pup body weights, and appearance and behavior observations. Macroscopic examinations were conducted on all F_0 animals with tissues and organs collected for microscopic examination and relative organ weight determination in accordance with the study protocol. All F_1 pups were examined macroscopically. Tissues and organs were collected for possible microscopic examination only

Responsible Care®
Good Chemistry at Work

88040000139/S

if deemed necessary by the gross finding. Histopathology of the control and high dose group F_0 animals is currently underway.

Decreased fertility was noted in the high dose group, as 6 of 12 animals with evidence of mating were gravid. The mid-dose group also showed signs of reduced fertility (2 of 11 animals with evidence of mating were gravid and 1 of 12 never conceived). Furthermore, there were effects regarding live litter size and pup survival in the high dose group. Only one of the litters from the 6 litters born in the high dose group survived to lactation day 4. The remaining pups (litters) in this dose group either died or were euthanized *in extremis*.

In addition to the observed reproductive and pups (litters) survival effects, there were effects noted on organ weights in both sexes. The organs affected included absolute and relative weights of the liver, epididymis and adrenal glands of males, and absolute and relative weights of the adrenal glands and relative weights of the ovaries of females. It was the organ weights of the mid and high dose groups that showed the most significant effects. The exception was the increases in female adrenal weights and relative ovary weights, which were observed in a significant dose-related manner for all 3 treated groups.

Sincerely,

John A. Biesemeier
Manager, Regulatory Toxicology
Regulatory Affairs

JAB/jab